

FORM PTO-1390 (Modified)
(REV 11-2000)

U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

ATTORNEY'S DOCKET NUMBER

TRANSMITTAL LETTER TO THE UNITED STATES
DESIGNATED/ELECTED OFFICE (DO/EO/US)
CONCERNING A FILING UNDER 35 U.S.C. 371

71745/56926

U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR

10/049737INTERNATIONAL APPLICATION NO.
PCT/GB00/03145INTERNATIONAL FILING DATE
August 15, 2000PRIORITY DATE CLAIMED
August 17, 1999

TITLE OF INVENTION

FLEXIBLE PIPETTE STRIP AND METHOD OF ITS USE

APPLICANT(S) FOR DO/EO/US

John CASSELLS, Thomas Richard Kerby EDWARDS, Michael John WITHERS, James LONG

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (24) indicated below.
4. ☐ The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c) (2))
 - a. ☒ is attached hereto (required only if not communicated by the International Bureau).
 - b. ☒ has been communicated by the International Bureau.
 - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
 - a. ☐ is attached hereto.
 - b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4).
7. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
 - a. ☐ are attached hereto (required only if not communicated by the International Bureau).
 - b. ☐ have been communicated by the International Bureau.
 - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
 - d. ☐ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
10. ☐ An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).
11. ☒ A copy of the International Preliminary Examination Report (PCT/IPEA/409).
12. ☒ A copy of the International Search Report (PCT/ISA/210).

Items 13 to 20 below concern document(s) or information included:

13. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
14. ☒ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
15. ☐ A **FIRST** preliminary amendment.
16. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
17. ☐ A substitute specification.
18. ☒ A change of power of attorney and/or address letter.
19. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
20. ☐ A second copy of the published international application under 35 U.S.C. 154(d)(4).
21. ☐ A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
22. ☒ Certificate of Mailing by Express Mail
23. ☒ Other items or information:

PCT/RO/101, PCT/1B/304, PCT/1B/308, PCT/IPEA/401, PCT/IPEA/402, PCT/IPEA/408
INTERNATIONAL PUBLICATION NUMBER WO 01/12330 A1
RESPONSE TO WRITTEN OPINION DATED 8/30/2001

U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR 1.492(a)(1) - (5)) : 10/049737		INTERNATIONAL APPLICATION NO. PCT/GB00/03145		ATTORNEY'S DOCKET NUMBER 71745/56926	
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24. The following fees are submitted: BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :				CALCULATIONS PTO USE ONLY	
<input type="checkbox"/> Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO \$1040.00					
<input checked="" type="checkbox"/> International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO \$890.00					
<input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO \$740.00					
<input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) \$710.00					
<input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) \$100.00					
ENTER APPROPRIATE BASIC FEE AMOUNT =				\$890.00	
Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).				\$0.00	
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	16 - 20 =	0	x \$18.00	\$0.00	
Independent claims	2 - 3 =	0	x \$84.00	\$0.00	
Multiple Dependent Claims (check if applicable). <input checked="" type="checkbox"/>				\$280.00	
TOTAL OF ABOVE CALCULATIONS =				\$1,170.00	
<input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27). The fees indicated above are reduced by 1/2.				\$0.00	
SUBTOTAL =				\$1,170.00	
Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492 (f)).				\$0.00	
TOTAL NATIONAL FEE =				\$1,170.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) (check if applicable). <input checked="" type="checkbox"/>				\$40.00	
TOTAL FEES ENCLOSED =				\$1,210.00	
				Amount to be: refunded	\$
				charged	\$

a. ☒ A check in the amount of **\$1,210.00** to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. _____ in the amount of _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. **04-1105** A duplicate copy of this sheet is enclosed.

d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

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David A. Tucker
 SIGNATURE

David A. Tucker
 NAME

27,840
 REGISTRATION NUMBER

February 15, 2002
 DATE

FLEXIBLE PIPETTE STRIP AND METHOD OF ITS USE

This invention relates to a system for manual and automated substance handling.

5 Single and multi-channel handling systems are widely used in drug discovery, medicine, biotechnology and chemistry. Both disposable and non-disposable pipettes are used, and these may be hand-held, mounted on a robot or integrated into a machine. Many such systems use pipettes.

10 Examples of pipetting systems using disposable pipette tips include hand-held single or multiple pipettors such as those manufactured by Eppendorf (Hamburg, Germany) and Gilson (Paris, France) and robot-mounted multiple pipettors such as those manufactured by Beckman Coulter Inc,
15 (Fullerton, California, USA). Disposable pipettes give the advantage that they eliminate cross-contamination from sample to sample and can also protect the user from the danger of coming into contact with infectious or hazardous substances. Whether in manual use or machine, systems
20 using disposable pipettes have to dispose of used tips and pick up new ones. With manual systems, a user may put individual tips onto the pipette by hand, but commonly fresh pipettes are picked up from a rack of tips. Pipettors are commonly used to load samples into microtitre
25 plates and the tip rack is chosen to match the pitch and layout of standard plates. Thus, tips may be arrayed in racks of 96 or 384 to match 96-well or 384-well plates.

With a manual pipettor, the user has to move the pipettor to a tip rack to pick up pipette tips. When the
30 pipette has been used, the operator then ejects the tip, usually into a waste container. This process has several disadvantages. The operator is required to make additional hand movements over and above the necessary operation of pipetting a sample from one container to another, thus
35 increasing fatigue and reducing throughput. The number of tips the user can access at any one time is limited by the number of racks that can be placed within arms reach. For

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very small volume devices, it is difficult for the user to align the pipettor with the new tip. As a result, pipettors for volumes of 2 microlitres or less are typically single channel devices.

5 Robotic liquid handling systems using disposable pipette tips have similar drawbacks. The speed of the cartesian robot or other automated device is limited by the need to accelerate, move and stop heavy mechanical systems from tip rack to sample and then to waste. The number of
10 liquid handling steps that can be performed in a single batch is limited by the number of tip racks that can be placed within reach of the robot. The precisional accuracy required to align sub-microlitre pipette tips has precluded the use of such devices in large arrays. Another
15 disadvantage is the cost of the racks used to support the tips.

20 An alternative approach is the use of non-disposable devices, singly or in arrays. Examples of single hand-held devices are the precision syringes for low volume liquid handling manufactured by Hamilton and SGE. The barrel is typically made of glass and the syringe is made of metal, sometimes with a plastic or elastomeric piston seal. Being precision devices made of expensive materials these syringes are too expensive to be disposable. Several
25 manufacturers, most notably Robbins Scientific (Sunnyvale, California, USA) and Tomtec (Hamden, Connecticut, USA) manufacture liquid handling systems with 96 or 384 such syringes in a common array. Non-disposable liquid handling devices have the benefit that it is not necessary to pick
30 up and dispose of tips, however this advantage is to a large part negated by the need to wash the syringes between additions to avoid cross-contamination between samples. The need to perform this wash step means that liquid handling systems that use non-disposable syringes have
35 throughputs that are generally comparable to systems using disposable tips, and can be slower if several washes are required. The choice between disposable tips and re-usable

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syringes is usually made on economic grounds or on the absolute requirement to eliminate cross-contamination. Re-usable syringes are perceived to be cheaper to run than disposable tips. Current disposable tips are expensive because of the need to provide these in a rack. When considering the true running cost of systems using non-disposable syringes it is important to take account of the cost of buying and disposing of the washing solvent and the cost of frequently replacing the syringe seals. In some cases, particularly in DNA amplification, it is necessary to guarantee zero cross-contamination even to the single molecule level. This can never be guaranteed with any system that relies on washing between transfers.

A common drawback with all currently existing multi-channel parallel pipetting systems is that each pipette cannot be individually addressed. Thus it is not possible when using, for example, a 96-pipettor array to add a reagent to all 96 wells of a microplate and then to add a second reagent to a chosen sub-set of the 96 wells with the same pipettor array. Even if the pistons in a 96 syringe array could be driven independently, it would still be necessary to immerse all 96 needles in the plate from which a sample was being transferred, thus leading to the possibility of wastage or carry-over.

The present invention provides a liquid handling system in which the pipettes may be disposable or re-usable and where the requirement to pick tips from a rack is eliminated. Furthermore, the present invention offers a means of high-speed sample transfer in a system that has full addressability for the pipette array. The system is compatible with low cost disposable devices.

According to the invention there is provided a strip of sampling devices comprising:

a strip of flexible material

an array of sampling devices joined to the strip to form a bandolier.

5 The flexible strip may have sprocket holes to drive and align the sampling devices. The devices may be of a positive displacement type having a barrel and piston, or may be of an air displacement type having a barrel (typically a cylindrical capillary or conical plastic tip) open at both ends or may be a sampling pin. It may be arranged so that all of the devices are held in the same plane and a hinged region is provided at each device to allow single or multiple devices to be hinged away from the general plane of the strip and thus be made available selectively.

10 The strip may be constructed of any suitable single or combination of materials such as plastic, paper or metal. The sampling device may be constructed of any suitable single or combination of materials such as plastics material, elastomer, metal, glass or ceramic. Alternatively, the sampling device and strip may be of unitary construction in a single material (preferably plastics material).

20 According to the present invention, there is also provided a method of substance sampling and dispensing, the method comprising the steps of:

25 feeding a strip, on which sampling devices are mounted, from a supply reel to an aspirate/dispense head; positioning one or more of the sampling devices ready for sampling;

taking a sample;

dispensing the sample; and

feeding the used sampling device to a waste container.

30 The method may be performed with two or more aspirate/dispense heads at one time.

Plural aspirate/dispense heads may be used in sequence so that multiple aspirations and multiple dispenses may be supported.

35 According to the present invention, there is further provided a substance sampling and dispensing system comprising:

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an aspirate/dispense head;
a supply reel for feeding to the aspirate/dispense head a continuous strip on which one or more sampling devices are mounted; and

5 positioning means for positioning the one or more sampling devices ready for sampling individually or in parallel.

The system may comprise a reel or stuffing box to accept used sampling devices.

10 The system may comprise further aspirate/dispense heads for receiving the strip prior to dispensing a sample.

The invention has particular benefits. A prior art pipetting apparatus will typically pick a pipette tip from a rack of tips, perform an aspiration at one location and
15 dispense liquid to another before ejecting the tip to take a fresh one. The tips are located in different positions in a rack, typically 96 at a time. The robot has to be programmed for each tip position and the tips must be accurately positioned. This is difficult and problems can
20 be experienced in tip pick and drop. The number of tips that can be accessed by the robot is limited to the number which can be accommodated in the area within the robots reach. The speed of pipetting is limited by the distance that the robot has to travel, the need for positional
25 accuracy and the need to accelerate and stop a heavy robot.

The method and apparatus of the present invention solves these problems. The sampling apparatus can be fed continuously with fresh sampling devices from a remote reel. A fresh sampling device is fed automatically to an
30 aspirate/ dispense head and is positioned to take a sample. The sampling device strip is always in contact with the robotic system, eliminating alignment problems. The need to travel to a tip rack position is eliminated, as is the capacity limitation dictated by the apparatus operating
35 envelope. As the sampling device strip has very low mass it can be accelerated, moved and stopped much faster than

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a robot leaving the aspirate and dispense heads having only to travel short distances.

Furthermore, the method of the invention may be applied across many actuators (aspiration and dispense) with the sampling device strip running between them. After the first aspiration, the full sampling device then leaves the aspirate head and travels to a dispense head where an aliquot of the sample is dispensed. The sampling device may then continue on to further dispense heads to dispense further aliquots, and then on to a waste reel. This process enables one-to-many and many-to-one reformatting at high speed.

This system provides the benefits listed above when operating the method of the invention. The system has the ability to select an array of any number of sampling devices from 1 to the maximum number of sampling devices the head can address which allows for the process of 'cherry picking'. Conventional multi-channel liquid handling systems present the whole array of sampling devices at once into the sample. It is therefore not possible with, for example a 384-way syringe array (of the Tomtec or Robbins Scientific type) to pick a single compound from a 384-well plate. This process is important in follow-up for drug discovery. The present invention allows for a single sampling device or any number of sampling devices to be 'selected' by moving it through 90 degrees from the plane of the strip, thus allowing individual samples to be taken.

One example of the present invention will now be described with reference to the accompanying drawings, in which:

Figure 1 shows an array of sampling devices joined to a backing strip;

Figure 2 is a perspective view of a number of sampling devices selectably addressed for use;

Figure 3 is a diagrammatic view of a two-head liquid handling system according to the invention; and

Figure 4 is a perspective view of the two-head liquid handling system of figure 3.

Referring to figure 1, an array of sampling devices 1 (in this case positive displacement pipettes) is joined to a backing strip 2 at a defined pitch (in this case 4.5 mm to match 384 and 1536-well plates). Sprocket holes 5 are provided to drive the tape. A hinge region 3 is incorporated into the backing strip 2 to allow each pipette 1 to be folded through ninety degrees to the plane of the backing strip. Figure 2 illustrates the benefit of this hinge region and motion. The strip is held flat above a target microplate. By rotating the pipette tips through ninety degrees about the hinge region 3 only the selected tips can access wells in the plate, and furthermore the rear of each pipette 6 is made more accessible to an actuator.

As shown in Figure 3, an actuator 14 can grip the back of the pistons 6 to operate the positive displacement pipette 1. Or, if the pipettes are of the air displacement type, an array of nozzles 11 may be brought down to mate with the rear of the pipettes 1.

In this example, any number of pipettes 1 may be selected for operation. The pipettor heads 7,8 may be continuously supplied with pipettes 1 from a reel 12 some distance from the pipettor. A single pipettor head 7 may be used for both aspiration and dispense. In this case the invention gives the advantages of an essentially unlimited supply of pipette tips and the elimination of the need to travel to a location to pick or discard tips. Further benefits are obtained by using multiple pipettor heads 7,8. Figures 3 and 4 show two heads being used. A first head 7 selects pipettes and aspirates a liquid from wells in a microplate 9 into those pipettes. The filled pipettes 13 then travel on to the second head 8, which again selects the pipettes and then delivers part or all of their contents to a continuous tape of wells 10. This may alternatively be a microplate. In this way, the heavy

mechanical components are only required to move up and down. The low mass pipettes travel at speed between the heads.

5 A sampling device tape with a continuous series of
sampling devices on a 4.5-mm pitch can be used to access
one row of 16 wells of a 384-well plate at once. By
selecting alternate sampling devices, the same tape could
access 8 wells of a 96-well plate (9mm pitch) and so on.
10 This ability to temporarily orientate individual components
is not a feature found in other systems using bandoliered
components such as resistors, capacitors and bullets.

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CLAIMS

1. A method of substance sampling and dispensing, the method comprising the steps of:
- 5 feeding a strip, on which sampling devices are mounted, from a supply reel to an aspirate/dispense head; positioning one or more of the sampling devices ready for sampling;
- taking a sample;
- 10 dispensing the sample; and
- feeding the used sampling device to a waste container.
2. A method according to claim 1, performed two or more aspirate/dispense heads such that sampling devices aspirate
- 15 samples at one head and then travel to a subsequent head to perform further aspiration or dispensing.
3. An array of sampling devices comprising:
- a strip of flexible material
- 20 an array of sampling devices joined to the strip to form a bandolier.
4. An array according to claim 3, wherein a hinge region is incorporated in the strip to allow some or all of the
- 25 sampling devices to be folded away from the plane of the strip or other sampling devices or the strip.
5. An array according to any of the preceding claims 3 or 4, wherein sprocket holes are incorporated in the strip to
- 30 facilitate drive and indexing of the strip.
6. An array according to any of claims 3 to 5, wherein the body of each sampling device is used as a gear track to facilitate drive and indexing of the strip.

7. An array according to any of claims 3 to 6 wherein the sampling devices are positive displacement pipettes.

8. An array according to any of claims 3 to 6, wherein
5 the sampling devices are air displacement pipette tips.

9. An array according to any of claims 3 to 6, wherein the sampling devices are capillaries.

10 10. An array according to any of claims 3 to 6, wherein the sampling devices are sampling pins.

11. A substance sampling and dispensing system comprising:
an aspirate/dispense head;
15 an array according to any of claims 3 to 10; and
positioning means for positioning the one or more
sampling devices ready for sampling individually or in
parallel.

20 12. A system according to claim 11, further comprising an actuator to fold, in use sampling devices away from the plane of the strip or other sampling devices on the strip.

25 13. A system according to claim 11 or 12, further comprising an actuator for selecting, in use one or more sampling devices at will from the array.

30 14. A system according to any of claims 11 to 13, further comprising at least one more actuator to aspirate or dispense samples from the same sampling devices.

15. A system according to any of claims 11 to 14, wherein the strip of sampling devices is fed from a reel or fan-fold box.

16. A device according to any of claims 11 to 15, wherein the strip of used sampling devices are fed to a waste container or reel.

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Figure 1

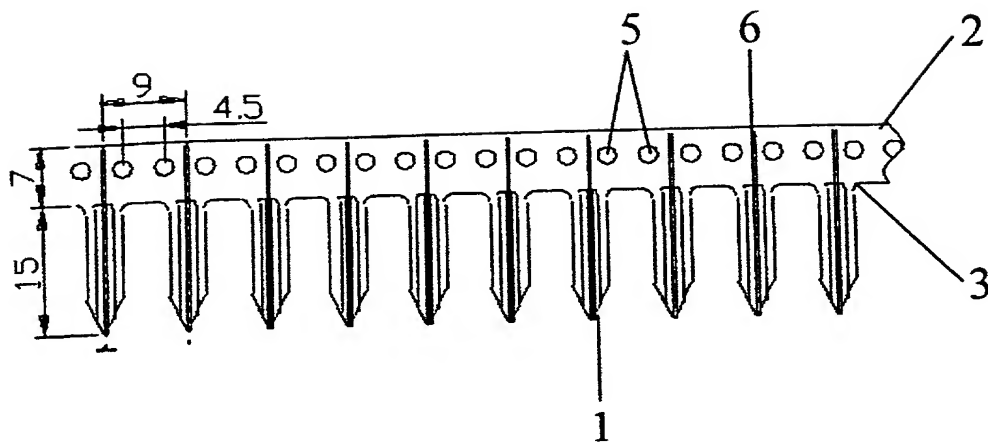


Figure 2

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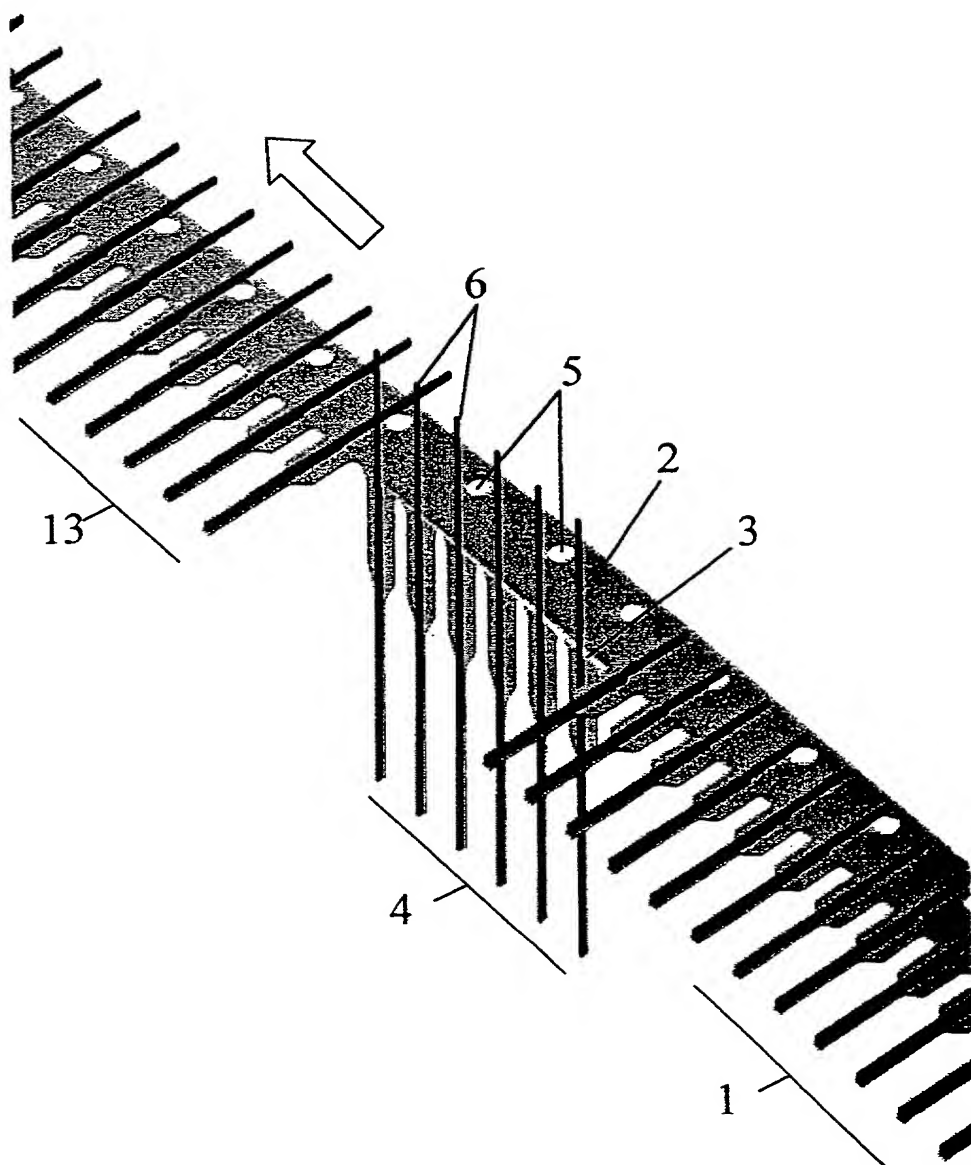


Figure 3

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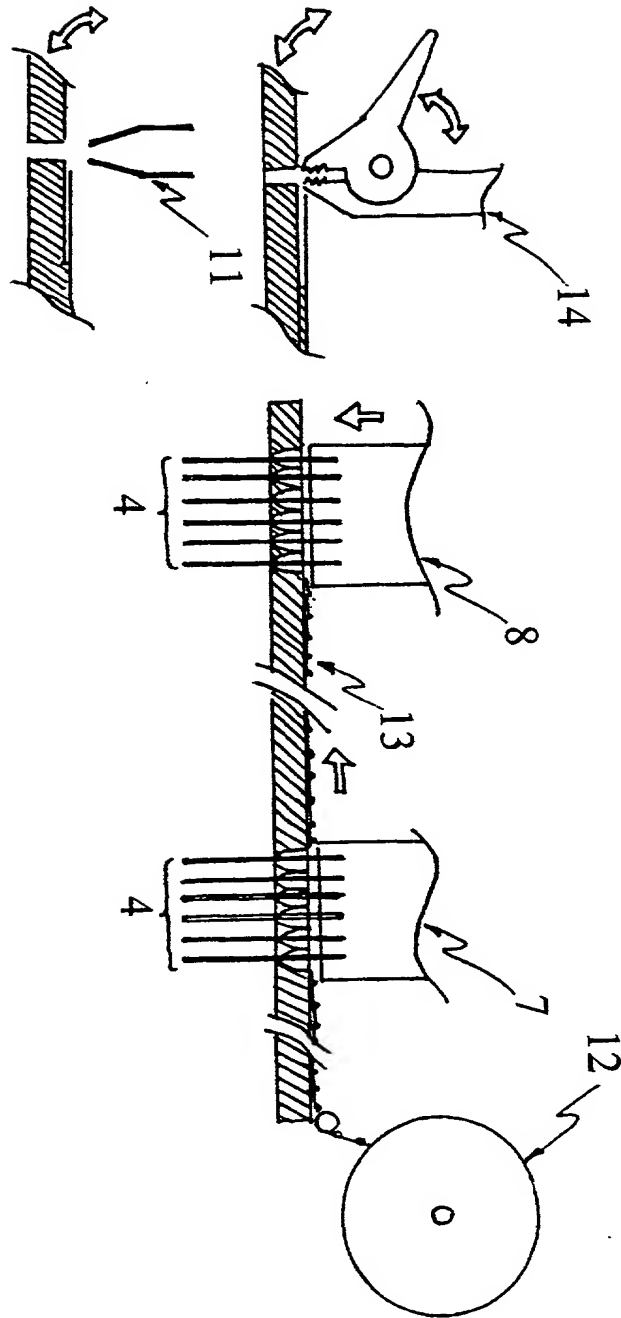
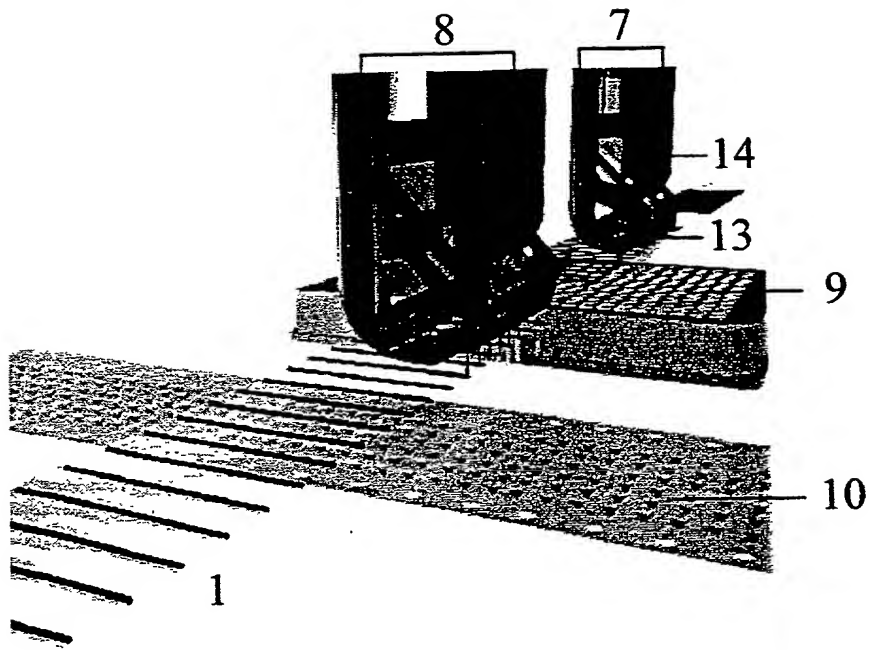


Figure 4



DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that: My residence, post office address and citizenship are as stated below next to my name. I believe I am the original, first and sole inventor (if only one name is listed at 201) below or an original, first and joint inventor (if plural names are listed at 201-206 below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

FLEXIBLE PIPETTE STRIP AND METHOD OF ITS USE

which is described and claimed in:

☐ the specification attached hereto.

☐ the specification in U.S. Application Serial Number _____, filed on _____.

☒ the specification in PCT international application Number, PCT/GB00/03145 filed on August 15, 2000; and was amended on _____.

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a). I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed.

Prior Foreign/PCT Applications and Any Priority Claims Under 35 U.S.C. §119:			
Application No.	Filing Date	Country	Priority Claimed Under 35 U.S.C. §119?
99306463.3	August 17, 1999	Europe	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO

I hereby claim the benefit under 35 U.S.C. §120 of any United States application(s) or PCT international application(s) designating the United States of America that is/are listed below, and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of 35 U.S.C. §112, I acknowledge the duty to disclose material information as defined in 37 CFR §1.56(a) which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application:

Prior U.S. Applications or PCT International Applications Designating the U.S-Benefit Under 35 U.S.C. §120					
U.S. Applications			Status (Check One)		
Application Serial No.	U.S. Filing Date		Patented	Pending	Abandoned
PCT Applications Designating the U.S.					
Application No.	Filing Date	U.S. Serial No. Assigned			

CLAIM FOR BENEFIT OF PRIOR U.S. PROVISIONAL APPLICATION(S)
(35 U.S.C. §119(e))

I hereby claim the benefit under Title 35, United States Code, §119(e) of any United States provisional application(s) listed below:

Applicant	Provisional Application Number	Filing Date

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) with full powers of association, substitution and revocation to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

Peter F. Corbin (Reg. No. 33,560)	Robert L. Buchanan (Reg. No. 40,937)	Susan M. Jensen (Reg. No. 42,693)
David G. Cimbala (Reg. No. 27,076)	Peter J. Marino (Reg. No. 26,766)	Christina C. O'Neil (Reg. No. 35,256)
George W. Neuner (Reg. No. 26,964)	Carl Z. Leven (Reg. No. 38,227)	Lisa Heston Swinney (Reg. No. 44,308)
Josiah M. Durkin (Reg. No. 31,003)	William J. Polky, Jr. (Reg. No. 35,487)	David A. Tucker (Reg. No. 27,890)
George W. Harwell, III (Reg. No. 42,632)	Richard Ross (Reg. No. 45,053)	T. Carter Pladger (Reg. No. 29,124)
Kathryn A. Asha (Reg. No. 34,001)	John B. Alexander (Reg. No. 45,392)	Danaz Ross (Reg. No. 45,281)

SEND CORRESPONDENCE TO: Dike, Bronstein, Roberts & Cushman Intellectual Property Practice Group Edwards & Angell, LLP P. O. Box 9169 Boston, Massachusetts 02209	DIRECT TELEPHONE CALLS TO: David A. Tucker (617) 517-5508
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1 8 0 0 1	FULL NAME OF INVENTOR	LAST NAME Cassells	FIRST NAME John	MIDDLE NAME
	RESIDENCE & CITIZENSHIP	CITY Royston GBX	STATE OR FOREIGN COUNTRY United Kingdom	COUNTRY OF CITIZENSHIP United Kingdom
	POST OFFICE ADDRESS	POST OFFICE ADDRESS c/o The Technology Partnership PLC Melbourn Science Park Cambridge Road Melbourn, Royston, Hertfordshire Royston Hertfordshire, United Kingdom SG8 6EE		
2 0 2	FULL NAME OF INVENTOR	LAST NAME Edwards	FIRST NAME Thomas	MIDDLE NAME
	RESIDENCE & CITIZENSHIP	CITY Cambridge GBX	STATE OR FOREIGN COUNTRY United Kingdom	COUNTRY OF CITIZENSHIP United Kingdom
	POST OFFICE ADDRESS	POST OFFICE ADDRESS 7 Leys Walk Hauxton Cambridge United Kingdom CB2 5HZ		
3 0 3	FULL NAME OF INVENTOR	LAST NAME Withers	FIRST NAME Michael	MIDDLE NAME John
	RESIDENCE & CITIZENSHIP	CITY Cambridge GBX	STATE OR FOREIGN COUNTRY United Kingdom	COUNTRY OF CITIZENSHIP United Kingdom
	POST OFFICE ADDRESS	POST OFFICE ADDRESS 17 Highfield Road Cambridge United Kingdom CB4 9PF		

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300

201	FULL NAME OF INVENTOR	LAST NAME	FIRST NAME	MIDDLE NAME
	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP
	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY AND ZIP CODE
202	FULL NAME OF INVENTOR	LAST NAME	FIRST NAME	MIDDLE NAME
	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP
	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY AND ZIP CODE
203	FULL NAME OF INVENTOR	LAST NAME	FIRST NAME	MIDDLE NAME
	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP
	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY AND ZIP CODE
204	FULL NAME OF INVENTOR	LAST NAME	FIRST NAME	MIDDLE NAME
	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP
	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY AND ZIP CODE
205	FULL NAME OF INVENTOR	LAST NAME	FIRST NAME	MIDDLE NAME
	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP
	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY AND ZIP CODE
206	FULL NAME OF INVENTOR	LAST NAME	FIRST NAME	MIDDLE NAME
	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP
	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY AND ZIP CODE

I hereby further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Signature of Inventor 201	Signature of Inventor 202
<i>Edu M. Correll</i>	<i>James Long</i>
Date: 7-2-2002	Date: 8-02-02
Signature of Inventor 203	Signature of Inventor 204
<i>Ullrich</i>	<i>J Long</i>
Date: 8/2/02	Date: 8-2-02
Signature of Inventor 205	Signature of Inventor 206
Date:	Date: